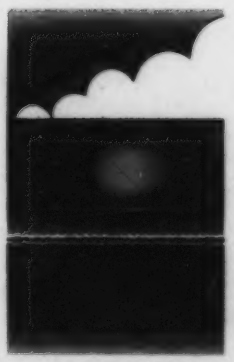
A STANDARD FOR N-NITROSODIMETHYLAMINE (NDMA)

A recommendation to the Minister of the Environment

ACES
Advisory Committee on Environmental Standards
Comité consultatif sur les normes environnmentales



A STANDARD FOR N-NITROSODIMETHYLAMINE (NDMA)

A recommendation to the Minister of the Environment

Prepared by ACES

ACES Report 92-01
January 1992
ISBN: 0-7729-9367-X

Cette publication technique n'est disponible qu'en anglais.

92-05028/

Table of Contents

	Page
Referral	1
Recommendation for a Maximum Acceptable Concentration for NDMA	1
Background	2
Public Health Significance	3
What is NDMA	3
Sources of Exposure to NDMA	3
Potential Adverse Health Effects of NDMA	4
Internal Review	4
Public Consultation Process	5
Review of Public Comment	6
Zero Discharge	7
Contribution from Other Sources	8
Measurement - Detection Limit	9
Cost - Economic Considerations	10
Approach - Model Used	11
Consideration of Synergistic Effects	13
Enforcement	13
Other Areas to Investigate	14
General Process - Format	14
Summary of Recommendations	16
References	17

Appendices

1 Summary Tables of Public Comments
2 List of Participants
3 NDMA Sampling Results
4 Models Used in Risk Assessment
5 Summary of the Risk Assessment for NDMA as presented at the Environmental Appeal Board Hearing
6 Summary of NDMA Guidelines in Other Jurisdictions
7 Background Material on NDMA

Referral

On August 9, 1991, Ruth Grier, Minister of the Environment requested that ACES (Advisory Committee on Environmental Standards) consult with the public on the Ministry of the Environment's Interim Maximum Acceptable Concentration (IMAC) 9 parts per trillion (ng/L) for the chemical N-nitrosodimethylamine (NDMA) in drinking water and recommend a Maximum Acceptable Concentration (MAC).

Recommendation for a maximum acceptable concentration for NDMA

ACES recommends that the maximum acceptable concentration for NDMA be set at 9 ppt as proposed. ACES further recommends that, because NDMA is a probable human carcinogen, the standard be reviewed in five years with the goal of reducing the tolerable limit towards zero as the technology to detect NDMA at very low levels improves.

Background

In November, 1989, the Ministry's Drinking Water Surveillance Program (DWSP) detected the first high concentration of NDMA in drinking water in Ontario at Elmira. No NDMA was detected (using a detection limit of 50 ppt) in similar DWSP studies at over 40 locations across Ontario.

An Interim Maximum Acceptable Concentration (IMAC) of 14 parts per trillion (ppt) was adopted by the Ministry to reduce NDMA discharges and a control order was issued to Uniroyal Chemical Ltd. The 14 ppt IMAC was based on readily available NDMA information as a temporary measure taken to reduce discharges until a more in-depth analysis could be conducted.

An Expert Committee was established by the Ministry in May, 1990 to identify potential guideline numbers and associated risk levels based on health consideration. All pathways of exposure to NDMA via air, water, soil, diet and consumer products were evaluated. The health risk of NDMA exposure at various levels over a lifetime (incremental lifetime cancer risk) was assessed. The Scientific Criteria Document (Ontario Ministry of the Environment 1991a) and the Rationale Document (Ontario Ministry of the Environment 1991b) were produced as a result of these deliberations.

After this review, the Ministry of the Environment adopted a more stringent IMAC for NDMA of 9 ppt. The Minister then requested that ACES carry out public consultation on the more stringent IMAC and recommend a Maximum Acceptable Concentration.

Public health significance

What is NDMA

NDMA is an organic compound belonging to the family known as nitrosamines. It is a chemically stable liquid at room temperature.

NDMA was once produced for use as an intermediate in the manufacture of rocket fuel, but it no longer has any commercial uses. It is produced as an inadvertent by-product of industrial processes that use amines and nitrites under acidic conditions. It may be present in the discharges from rubber manufacturing, leather tanning, pesticide manufacturing, food processing, foundries, dye manufacturing and as a result also may be found in sewage treatment plant effluent.

Sources of exposure to NDMA

There appear to be many potential sources of exposure to NDMA. Perhaps the largest source is through food. NDMA is present in some foods such as certain cheeses, cured meat products, smoked or salted fish and several alcoholic beverages. It also can be formed in the stomach when foods containing secondary amines (such as fish or meat) are consumed with foods containing nitrite or nitrate (such as spinach). A chemical reaction can take place in the acidic environment of the stomach to form NDMA from these foods, but the reaction can also be inhibited in the presence of Vitamin C (found in orange juice) or other antioxidants.

In addition to food, other potential sources of exposure to NDMA are certain drugs, pesticides, and tobacco smoke. Formation of NDMA can occur during the treatment of drinking water (See Appendix 3).

NDMA present in the air degrades rapidly into dimethylamine on exposure to ultraviolet radiation in sunlight and, consequently, levels in Ontario air samples have been generally non-detectable.

NDMA is very water soluble and may be ingested in drinking water. If the drinking water is derived from surface waters, it is unlikely that the NDMA concentration will be significant as exposure to sunlight will result in its degradation. However, NDMA has the potential to migrate into groundwater, where its degradation is much slower.

Regardless of the source of exposure, NDMA is not expected to bioaccumulate.

Potential adverse health effects of NDMA

NDMA is classified as a ***probable human carcinogen*** by the World Health Organization's International Agency for Research on Cancer and by the United States Environmental Protection Agency. This designation is based on the fact that NDMA has been shown to produce cancer in over 40 animal species in which it has been tested including mammals, birds, fish and amphibians. It is metabolised similarly by animal and human tissues. NDMA is a potent carcinogen with tumors arising primarily in the liver, kidney and respiratory tract. NDMA also has been shown to produce necrotic, hemorrhagic and cirrhotic alterations in the liver.

For more detailed discussion of the toxicology of NDMA see: Scientific Criteria Document for Multimedia Standard Development No. 01-90 N-Nitrosodimethylamine. (Ontario Ministry of the Environment 1991a)

Internal review

Upon receipt of the Scientific Criteria Document and the Rationale Document from the Ministry, ACES undertook its own internal review to determine whether the documentation was adequate to frame an effective public consultation process.

ACES also reviewed toxicological evidence that was presented at the Environmental Appeal Board hearings of an appeal of the control order issued to Uniroyal Chemical Ltd. in Elmira to limit the concentration of NDMA generated in its waste streams and subsequently discharged. This material provided many insights into derivation of a risk assessment for NDMA which were relevant to ACES' review, however, the basis of the appeal was the 14 ppt IMAC and the rationale for the selection of this number was different than the rationale used for the 9 ppt which was the subject of the ACES consultation. (A summary of the Risk Assessments for NDMA as presented at the Environmental Appeal Board hearing is shown in Appendices 4 and 5. A summary of NDMA guidelines in other jurisdictions is shown in Appendix 6.)

ACES concluded that the documentation presented in the Scientific Criteria Document (Ontario Ministry of the Environment 1991a) and the Rationale Document (Ontario Ministry of the Environment 1991b) was adequate to proceed with public consultation.

Public consultation process

A mailing list was compiled from several different mailing lists provided by the Ministry of the Environment to which names from the following groups were added: industry, environmental organizations, labour unions and Elmira area residents/groups.

A package of background material (See Appendix 7) was prepared including an information sheet on NDMA, a copy of the advertisement that appeared in newspapers (which included the questions being posed) and a brochure on ACES and the public consultation process. A list of scientific documents was provided that could be distributed upon request. Everyone was provided with a postage paid return envelope to encourage participation. This package was sent to approximately 5,500 people between September 20, 1991 and September 27, 1991.

The questions posed were kept to a minimum to encourage participation and to focus responses. The questions were:

1. Is the proposed standard acceptable?
2. If not, what is the basis for your finding the proposed level unacceptable?
3. Do you have an alternative level to propose?

Additional comments also were encouraged.

A second mailout was sent to 32 individuals and companies who had been identified as having a special interest in the review of NDMA but had not yet responded to the first mailout.

In order to reach members of the potentially interested public who might not be on the mailing list, an advertisement, which included the above questions, appeared once in each of 23 newspapers across the province during the weeks of September 28th to October 6th. An advertisement also appeared in the Ontario Gazette on September 28th and on the Web Network on September 27th. (The Web Network is a communications network which is subscribed to by many different organizations including many environmental groups from around the world).

The deadline for responses to the three questions was November 27, 1991.
Any requests for a public meeting had to be received by November 12, 1991.

Review of public comment

A total of 573 requests for additional information were received in response to the initial mailout and advertisements. These respondents were sent the Scientific Criteria Document and the Rationale Document (Ontario Ministry of the Environment 1991a and 1991b). Additional information was available at the ACES office.

A total of 81 responses were received dealing with various aspects of the rationale for setting an IMAC of 9 ppt for N-nitrosodimethylamine. A summary listing of respondents is attached as Appendix 2. Only one respondent thought that there was a need for a public meeting.

The responses were divided into four categories depending on how they answered the question regarding acceptability of the proposed standard. This summary is presented in Table 1.

Table 1. Summary of Responses

Comment	No.	%
Yes, the proposed standard is acceptable	25	31
Question not answered directly	16	20
No, the proposed standard is not acceptable - the level should be lower	13	16
No, the proposed standard in not acceptable - the level should be higher	27	33
Total comments received	81	100

The proposed standard was deemed acceptable by 31% of the people. The standard was deemed unacceptable by 49% of the respondents, 16% recommending that the level be lower and 33% recommending that the level be higher. The question was not answered directly by 20% of the respondents, most of whom felt that they were not qualified to comment or did not have enough information on which to base an opinion; nonetheless, many of these respondents provided useful comments on the process and other areas for further investigation.

In reviewing the comments submitted, every response was considered carefully. Their contents ranged from form letters or very brief comments on the proposed standard through to detailed technical submissions. When analyzing the responses, a number of general issues were identified (See Appendix 1). Many respondents addressed more than one issue.

These issues were categorized as follows:

Zero Discharge
Contribution from Other Sources
Measurement - Detection Limit
Cost - Economic Considerations
Approach - Model Used
Consideration of Synergistic Effects
Enforcement
Other Areas to Investigate
General Process - Format

Zero Discharge

A number of respondents (23%) felt that this standard is a good place to start to implement a policy of **zero discharge** to minimize the amount of poisons or contaminants in the drinking water. Certain respondents who agreed with the proposed limit felt, nevertheless, that the level should be re-examined with the intent of reduction within a certain interval of time. The most frequently mentioned interval was five years.
The provisions of the Great Lakes Water Quality Agreement, between Canada and the United States of America and administered by the International Joint Commission, regarding zero discharge and virtual elimination were cited as guiding principles. Respondents also mentioned the policy of the United States Environmental Protection Agency to set zero maximum contaminant level goals for suspected carcinogens.

Response by ACES
ACES strongly agreed with the principle of virtually eliminating persistent toxic substances from the environment. NDMA is persistent in ground water and is a probable human carcinogen.

Recommendation
ACES recommends that the maximum acceptable concentration for NDMA be set at 9 ppt as proposed. ACES further recommends that, because NDMA is a probable human carcinogen, the standard be reviewed in five years with the goal of reducing the tolerable limit towards zero as the technology to detect NDMA at very low levels improves.

Contribution from other sources

Contribution of NDMA from other sources was cited by 33% of respondents to be of concern.

Other sources of exposure mentioned included food, tobacco smoke and endogenous production. The majority of respondents indicated that the other sources overwhelmed the contribution from drinking water by a large amount.

The respondents that wanted a lower level of NDMA in drinking water used this statement as justification for suggesting that since the already significant amounts of NDMA from other sources of exposure pose a risk, no additional amounts of NDMA should be allowed in the drinking water.

The respondents favoring a higher acceptable concentration of NDMA in drinking water felt that since water provides such a minor contribution, emphasis should be placed on sources that provide a more significant contribution. A number of respondents expressed concerns that while endogenous production was mentioned as being significant, no efforts were made to incorporate this route into the risk assessment. Furthermore, some respondents felt that there was no evidence to suggest that incremental amounts were harmful.

Concerns were expressed about the amount of NDMA that could be produced by sewage treatment plants in the normal course of operation. Caution was advised that by setting a very low level, it may become impossible to provide drinking water which complies with this level and it may not be possible to effectively treat waste water and still comply with this level.

Response by ACES

ACES agreed that food constitutes a very significant contribution to the total body burden of NDMA and felt that this is an area that merits further close investigation by Health and Welfare Canada in terms of potential for reduction. However, ACES was of the opinion that since contributions from other sources are high, it is likely that an incremental increase in dose would lead to a notable increase in risk. It also is possible that the liver's detoxification mechanisms are just able to cope with the dietary level of NDMA exposure and any additional exposure through drinking water would overwhelm these systems. Furthermore, people have a wide range of choice in the foods they consume, but usually little or no choice in their source of drinking water. So it is important to keep the drinking water as "pure" as possible. Finally, the Provincial Government has jurisdiction over drinking water, but not over food, so it is incumbent upon the Province to do what is in its power to protect the health of its citizens.

Recommendation

ACES recommends that the virtual elimination of known or suspected carcinogens from drinking water be a guiding principle in setting drinking water standards. ACES further recommends that agreement be obtained from Health and Welfare Canada to undertake measures which will result in the reduction of NDMA levels in food. ACES recommends that the Ministry regulate nitrate and nitrite levels in drinking water with the goal of reducing these precursors of endogenous formation of NDMA to the lowest levels possible.

Measurement - Detection limit

The issue of measurement and detection limit provoked a large number (36%) of comments from respondents.

The majority of the comments dealt with the belief that 9 ppt could not be measured with any degree of certainty and that very few labs were equipped and qualified to perform these analyses on a routine basis. Concerns were raised that there may not be a significant difference between 9 ppt and 14 ppt. There was also much discussion on the issue of detection limit versus reporting limit with various opinions on how much higher than the detection limit the reporting limit should be. Concern also was expressed that a sufficient monitoring survey of NDMA in drinking water had not been done to determine the extent of the issue.

Response by ACES

ACES agreed that there was a great deal of uncertainty in the meaningful measurement of specific levels of NDMA in the range being considered. It was felt that as a solution to this dilemma a presence/absence approach could be taken as was suggested by one of the respondents. The philosophy behind this strategy is that if NDMA is there, then a problem exists since it is a probable human carcinogen. The exact level is not the issue. A methodology would be specified and the Ministry would perform random quality assurance checks to ensure that data being generated are valid.

ACES notes that a further DWSP survey was conducted with a detection limit of 5 ppt to specifically examine areas where NDMA might be expected to be found on the basis of the type of drinking water treatment process used. (See Appendix 3).

Recommendation

ACES recommends that a more extensive drinking water survey be done throughout the province to identify any potential areas of higher concentration. ACES further recommends that the Ministry address the uncertainty around the meaningful measurement of specific levels of NDMA in the parts per trillion range.

Cost - Economic considerations

The issues of cost and economic considerations were raised by 38% of the respondents. Comments centered on the lack of an adequate consideration of costs and methods of removal in the documentation and also included concerns about the high cost of monitoring. Suggestions were made that reduction of NDMA levels should not be contemplated for a source as minor as drinking water, and that efforts could be better directed elsewhere.

A number of respondents felt that industry should be responsible for and be required to include the cost of treatment into the cost of their products. One respondent then went on to suggest that this might lead the consumer to re-examine the need for the product. One group felt that it was the taxpayers and not industry that had borne the brunt of the costs associated with contamination at Elmira; therefore, industry must be made to take more responsibility for its products and by-products.

Concerns were raised that it is very expensive and difficult to treat water with such low concentrations. This led some respondents to suggest that cost considerations should be factored into the determination of further efforts to control exposure through other sources, while others felt that the high cost of treatment provides the impetus to eliminate the substance entirely leading to implementation of zero discharge.

Response by ACES

ACES felt that there was a lack of consideration of economic implications associated with implementing a more stringent standard. This was further compounded by the lack of an adequate survey to determine the extent of NDMA contamination of drinking water in the province.

Recommendation

ACES recommends that an analysis be performed which includes determination and allocation of the costs associated with implementation of the standard, specifically, the costs of routine monitoring as well as prevention and treatment technology.

Approach - Model used

Comments on the model used to derive a risk assessment for NDMA were made by 14% of the respondents. These ranged from very general statements of agreement with the model to very specific and detailed concerns about assumptions used in the models and safety factors employed.

Concerns were expressed about the validity of using a dose-response model which intersects the origin when NDMA is ubiquitous at 1 ppt in the environment. The strength of the epidemiological data was questioned, and concerns were raised regarding potentially different responses in different biological systems. It was suggested that the dose used was too high and there was no evidence of carcinogenicity at lower levels. The lack of consideration of endogenous production was cited as a weakness.

In the Scientific Criteria Document (Ontario Ministry of the Environment 1991a), the risk assessment was derived by extrapolating from the very high doses used in the BIBRA (Brantom *et al.* 1978) animal study to the very low doses to which humans are exposed. This was done with the use of a mathematical model called the Weibull model. It was suggested that another model, the Linear Multistage model, may be more appropriate since it accounts for technological limitations and sampling error and may be the most conservative model.

Response by ACES

ACES considered these opinions as well as the more detailed analysis of the strengths and weaknesses of various models and assumptions which came out of the testimony at the NDMA control order appeal heard by the Environmental Appeal Board (see Appendices 4 and 5).

ACES felt that the Weibull model was the most appropriate since it makes use of all the data in the BIBRA study, which is the most comprehensive carcinogenesis data set available. The Weibull model has also been reported to be the best model for determining the parameter (time to tumour) (Portier *et al.* 1986 and Swenberg *et al.* 1991). It was felt that the biological response should be considered first and then an evaluation of technological limitations be made. Differences among species were not considered to be a major concern since nitrosamines seem to be one of the few chemicals that induce cancer in all species tested.

ACES felt that since exposure is already so high from other sources there is confidence in the dose response curve at the levels observed (See further discussion under **Contribution from Other Sources** and **Consideration of Synergistic Effects**).

ACES did, however, question three of the assumptions made in the Scientific Criteria Document in deriving the risk assessment for NDMA: (1) In analyzing the BIBRA study the Scientific Criteria Document used an average rat lifespan of 3 years. Some of the rats in this study were exceptionally long-lived. Two years is a universally used value and the Committee felt it would be more appropriate to use this value. (2) In the Scientific Criteria Document, a *de minimis* (negligible) risk level of 10^{-5} is used. This means that 1 additional cancer death among 100,000 people is considered to be a negligible increase and therefore, a risk that is acceptable. ACES agreed with the testimony presented to the Environmental Appeal Board hearing (Ontario Ministry of the Environment 1990[1]), in which it was pointed out that if the total *de minimis* risk from all sources is to be 10^{-5} then the risk for each individual component (eg. drinking water) must be less than 10^{-5}. ACES felt that a risk level of 10^{-6} would be appropriate for drinking water. (3) Finally, ACES questioned the use of the ***average*** water consumption value of 1.5 litres of water per day in deriving the risk assessment.

A 1981 report by Health and Welfare Canada suggests that about a third of the population consume more than 1.5 litres per day. Using a value of 2 litres per day, as recommended by the World Health Organization (1984) would protect about 83% of the population at the acceptable level of risk.

When the effects of altering these 3 assumptions are combined, as is shown in Appendix 5, the limit changes from 9 ppt to 11.6 ppt. As was discussed under **Measurement-Detection Limit**, these two values are so close that they cannot be distinguished with any degree of accuracy. Also, as discussed under **Zero Discharge**, the goal in standard setting for known or probable human carcinogens should be virtual elimination. Therefore, ACES feels that there is no need to change the standard for NDMA on the basis of these suggested alterations to the assumptions in the risk assessment.

Recommendation

ACES recommends that the following assumptions be used in deriving the risk assessment for future drinking water contaminant standards: length of average rat lifespan of 2 years, negligible risk level of 10^{-6} and the use of average water consumption of 2 litres per day.

Consideration of synergistic effects

A few respondents (6%) identified the lack of a process or vehicle to consider and evaluate synergistic effects. Concerns included the lack of knowledge about interactions among the large number of man-made chemicals in the environment.

Response by ACES

ACES agreed that this is an area of concern based on understanding of the potential for overloading the detoxification processes in the cells (see discussion under **Contribution from Other Sources**) and on the apprehension that synergistic effects of a multitude of contaminants may overwhelm cellular repair systems.

ACES felt that this provides further reason to keep levels of NDMA as low as possible in drinking water.

Recommendation

ACES recommends that levels of NDMA in drinking water be kept as low as possible due to concerns about synergistic effects. ACES recommends that further investigation into the synergistic effects of multiple contaminants become a priority for research supported by the Ministry.

Enforcement

Enforcement was mentioned by 5% of the respondents. Concerns were raised about the high cost of enforcement which might compromise its effectiveness.

The respondents felt that any standard should be enforced and alternate sources of water be provided should the standard be exceeded.

Response by ACES

Standards incorporated into Statutes or Regulations are enforceable by law, unlike guidelines or objectives.

Recommendation

ACES recommends that standards be incorporated into Statutes and Regulations as a mechanism for strong environmental protection. Alternate sources of water should be provided where these limits are exceeded.

Other areas to investigate

A few respondents (6%) made suggestions about other areas that should be investigated. Suggestions were made that studies on interactions between NDMA and soil and vegetation should be explored as these are important areas where information is lacking.

Questions were raised as to whether there was any evidence of the effects on immature/growing systems and whether infants or children were at greater risk.

Response by ACES
ACES agreed that gaps in knowledge should be considered in the Ministry's priority setting for research.

Recommendation
ACES recommends that gaps in knowledge such as interactions of NDMA with soil and vegetation and risk assessment for sensitive groups in the population, such as children, be considered for further research.

General process - format

Comments on the general process-format were received from 42% of the respondents. The majority of these respondents appeared to appreciate the opportunity to provide input into the process of standard setting and expressed hopes that this process would be repeated with other contaminants. Some questioned whether the right process was being used given that the extent of the issue appears to be so narrow and geographically limited.

Other issues raised included suggestions that the limitations of the methodology were not clear enough and that a better separation should be made between fact and opinion in the documentation. It was suggested that a statement regarding the significance of higher levels of NDMA in drinking water was needed.

Response by ACES:
ACES agreed that a better explanation of the limitations of the methodology could be provided and gaps in the knowledge identified. In general, ACES was pleased with the process and with the extent and quality of responses received to the request for comment. About 14% of those who requested the information package actually commented. ACES felt that this degree of response was quite reasonable given the scientific nature of the material.

The process by which the standard was derived seems to be a rational one. ACES approved of the process and felt that the standard of 9 ppt was justifiable on the basis of this process.

Recommendation:

ACES recommends that the maximum acceptable concentration be set at 9 ppt as the process used in deriving the level was rational and acceptable. ACES further recommends that for future documents, a better explanation of the limitations of the methodology be provided and gaps in the knowledge identified.

Summary of recommendations

ACES recommends that the maximum acceptable concentration for NDMA be set at 9 ppt as proposed. ACES further recommends that, because NDMA is a probable human carcinogen, the standard be reviewed in five years with the goal of reducing the tolerable limit towards zero as the technology to detect NDMA at very low levels improves.

ACES recommends that the virtual elimination of known or suspected carcinogens from drinking water be a guiding principle in setting drinking water standards. ACES further recommends that agreement be obtained from Health and Welfare Canada to undertake measures which will result in the reduction of NDMA levels in food. ACES recommends that the Ministry regulate nitrate and nitrite levels in drinking water with the goal of reducing these precursors of endogenous formation of NDMA to the lowest levels possible.

ACES recommends that a more extensive drinking water survey be done throughout the province to identify any potential areas of higher concentration. ACES further recommends that the Ministry address the uncertainty around the meaningful measurement of specific levels of NDMA in the parts per trillion range.

ACES recommends that an analysis be performed which includes determination and allocation of the costs associated with implementation of the standard, specifically, the costs of routine monitoring as well as prevention and treatment technology.

ACES recommends that the following assumptions be used in deriving the risk assessment for future drinking water contaminant standards: length of average rat lifespan of 2 years, negligible risk level of 10^{-6} and the use of average water consumption of 2 litres per day.

ACES recommends that levels of NDMA in drinking water be kept as low as possible due to concerns about synergistic effects. ACES recommends that further investigation into the synergistic effects of multiple contaminants become a priority for research supported by the Ministry of the Environment.

ACES recommends that standards be incorporated into Statutes and Regulations as a mechanism for strong environmental protection. Alternate sources of water should be provided where limits are exceeded.

ACES recommends that gaps in knowledge such as interactions of NDMA with soil and vegetation and risk assessment for sensitive groups in the population, such as children, be considered for further research.

ACES recommends that the maximum acceptable concentration be set at 9 ppt as the process used in deriving the level was rational and acceptable. ACES further recommends that for future documents, a better explanation of the limitations of the methodology be provided and gaps in the knowledge identified.

References

Brantom, P.G., Grasso, P., Gangolli, S.D.G., Crampton, R.F.

1978. Dose response studies with dimethyl and diethylnitrosoamine in the rat. The British Industrial Biological Research Association, Carshalton, Surrey SM5 4DS, U.K. Unpublished report prepared for the British Ministry of Agriculture, Fisheries and Food.

Health and Welfare Canada.

1981. Tapwater Consumption in Canada. Environmental Health Directorate, Health Protection Branch.

Ontario Ministry of the Environment.

1990. Transcripts from File SWA.011.90, SWA.013.90, SWA.014.90. Environmental Appeal Board Hearing into the appeal by Uniroyal Chemical Ltd. of a control order under s. 32(1) and s.8 of the Ontario Water Resources Act. ([1] refers to testimony by Dr. R. Brecher).

1991a. Scientific Criteria Document for Multimedia Standard Development No. 01-90 N-Nitrosodimethylamine. Hazardous Contaminants Coordination Branch.

1991b. Rationale Document for the Interim Maximum Acceptable Concentration for N-Nitrosodimethylamine (NDMA) in Drinking Water. Hazardous Contaminants Coordination Branch.

Portier, C.J., Hedges, J.C. and Hoel, D.G.

1986. Age-specific models of mortality and tumour onset for historical control animals in the National Toxicology Program's carcinogenicity experiments. Cancer Research 46: 4372-4378.

Swenberg, J.A., Hoel, D.G. and Magee, P.N.

1991. Mechanistic and statistical insight into the large carcinogenesis bioassays on N-nitrosodiethylamine and N-nitrosodimethylamine. Cancer Research 51(23): 6409-6414.

World Health Organization.

1984. Guidelines for Drinking Water Quality.

APPENDIX 1

Summary Tables of Public Comments

EXPLANATION OF CODES USED IN SUMMARY TABLES OF PUBLIC COMMENTS	
Comment	Code
Yes, the proposed standard is acceptable	Y
Question not answered directly	YN
No, the proposed standard is not acceptable - the level should be lower	N<
No, the proposed standard in not acceptable - the level should be higher	N>

ZERO DISCHARGE			
	Comment	**Code**	**Respondent**
1	Why not try for a decrease gradually through the next 5 years?	Y	Individual
2	Level should be reviewed in 5 years and reset according to BATS as it is in MISA.	Y	Manitoba Hydro
3	The lower level is headed in the right direction. The level which should ultimately be legislated is zero.	Y	Hiram Walker & Sons, Windsor
4	Ultimately, it would be acceptable that all substances that are considered potentially carcinogenic or hazardous would be limited to zero.	Y	Dames & Moore, Canada
5	I would like to see a time limit - say 5 years. During that time industries that release NDMA would be required to research and develop means of production that significantly reduce/eliminate the release of NDMA. The aim would be zero contamination.	Y	Individual
6	Let's keep the standard as low as we possibly can.	YN	Individual
7	Let us remind you that the U.S. EPA recommends a zero concentration as the ultimate objective for this contaminant.	YN	Ministry of the Environment, Quebec
8	Not allow any traces of such a chemical in the drinking water until it can be conclusively proven to be of no significance.	N<	Z.I.P. Communications and Consulting, Cornwall
9	To permit small quantities of such a poison in public drinking water is a step up the ladder of betrayal to future generations.	N<	W.C. Investments, Elmira
10	I believe that pollution control should mean to bring nature back to its original state.	N<	Individual
11	We believe that there are already too many chemicals in our drinking water.	N<	Individual

12	What with the potential for this chemical to affect serious consequences on animals in the laboratory, there is reluctance to condone any level of NDMA in drinking water.	N<	Individual
13	Believes in zero discharge. Limits for carcinogens in drinking water must be set at zero or at the lowest limits possible.	N<	CAW Local 195 Environment Committee, Windsor
14	What should be striven for is zero discharge of NDMA, one of the more potent carcinogens.	N<	Centre for International Studies, University College of Cape Breton, Nova Scotia
15	Strongly supports zero discharge.	N<	Pesticide Action Group, Guelph
16	Proposes that zero discharge of toxic substances be the ultimate goal for defining the proposed guidelines.	N<	Individual
17	Supports zero discharge and the eventual elimination of toxic chemicals.	N<	Pesticide Action Group, Cambridge
18	The final goal for any such toxic substance must be zero discharge,	N<	Consumers' Association of Canada (Ontario)
19	Cite provisions of Great Lakes Water Quality Agreement regarding zero discharge and virtual elimination.	N<	Assuring Protection for Tomorrow's Environment, Elmira

This list does not include individuals who felt that the standard should be lower based on consideration of detection limits.

CONTRIBUTION FROM OTHER SOURCES			
	Comment	**Code**	**Respondent**
1	Can the amount in food be decreased? Are there plans underway?	Y	Paudash Lake Conservation Association
2	Multitude of potential sources including that of passive cigarette smoke.	Y	CANVIRO Analytical Laboratories Ltd., Waterloo
3	Cites NDMA incidence in tobacco smoke, cured meat products, etc. Mentions organic filter developed by self.	Y	Individual
4	Why is drinking water considered for guideline, when food is the main source?	YN	Individual
5	Provided information based on case study on NDMA produced in water treatment plants.	YN	Pollutech, Oakville
6	Cite high levels of NDMA in food and endogenous production. Question if concentrations in drinking water will have additional impact. Raise concerns about NDMA production in wastewater treatment plants.	YN	PUC of the City of Brantford
7	Raises questions of total impact on humans of multiple exposures.	N<	Individual
8	ACES should recommend followup study for exposure through food.	N<	CAW Local 195 Environment Committee, Windsor
9	Other avenues of exposure are known to exist.	N<	Pesticide Action Group, Cambridge
10	Exposure from food is significant.	N>	Blue Sky Research, Oakville
11	NDMA is present in many foods as well as produced in the body.	N>	Individual
12	Question the 9 ppt level when compared with relative abundance in food.	N>	Form letter from PUC (14X)

13	Since NDMA is present in many foods, and produced by the body, what evidence is there that incremental amounts are harmful? Cites tobacco smoke as one of the primary sources.	N>	Individual
14	Endogenous production estimates combined with intake from food, drink and tobacco are overwhelming when compared with amount in the water.	N>	Individual

MEASUREMENT - DETECTION LIMIT			
	Comment	Code	Respondent
1	Doubts that level could be measured with realistic accuracy.	Y	Individual
2	Consideration was given to the capability of measurement.	Y	Rohm and Haas, West Hill
3	Does not recognize that there is any significant difference between 9 and 14; therefore, change probably only raised public fears and increased project costs. Change should only be done if an order of magnitude change is being considered.	Y	CANVIRO, Waterloo
4	Representative of company that is developing analytical methods to facilitate measurement.	YN	Pylon Electronic, Ltd., Nepean
5	Finds that current level of detection is 150 ppt.	YN	Regional Municipality of Ottawa-Carlton
6	Concern that both 9 and 14 are equal to the detection limit of low resolution GC/MS system.	YN	Investigative Science Inc. and Six Nations Council
7	One wonders whether the 9 ppt is above the analytical detection limit or if it is equal to that limit.	YN	Ministry of the Environment, Quebec
8	This level reflects the level that current technologies can with some confidence detect and report on.	N<	Individual
9	Measuring this chemical is now possible to 1 ppt.	N<	Bruce Peninsula Environment Group, Lion's Head
10	Not acceptable because 9 is below detection limit of 10 ppt. in wastewater.	N>	Manitoba Research Council
11	Any standard should not be less than 10X the detection limit.	N>	Scott Maritimes Research Ltd., Nova Scotia

12	Is 1 ppt significantly different from 9 ppt? The detection limit must be demonstrable for a regulation to be meaningful. Address risk in an "uncontaminated environment" when NDMA is ubiquitous at 1 ppt.	N>	Blue Sky Research, Oakville
13	Data within a factor of 3-5 of detection limit are considered semi-quantitative and are flagged by MOE.	N>	Zenon, Burlington
14	Doubts ability of current methods of detection to accurately, reliably and consistently measure at 9 ppt.	N>	Individual
15	9 ppt is same as current limit of detection; therefore, accuracy will be low.	N>	American Water Works Association, Ontario Section
16	A routine monitoring method must be available before decisions to implement are made.	N>	Form letter from PUC (14X)

COST - ECONOMIC CONSIDERATIONS			
	Comment	Code	Respondent
1	Cost appears reasonable.	Y	RBW Graphics, Owen Sound
2	Cost of control was considered.	Y	Rohm and Haas Canada, Inc., West Hill
3	Industry should fund research into development of means that would reduce release of NDMA with aim of zero.	Y	Individual
4	Level should be something which is practical and within logical cost parameters.	YN	Township of Medonte
5	Need more information on treatment options and costs.	YN	Regional Municipality of Carlton
6	Concern about cost of achieving detection limit in lab measurement/analysis, require more expensive and less available high resolution systems.	YN	Investigative Science Inc., Six Nations Council
7	Cost consideration should be factored into determination of priority to further efforts to control potential risk associated with exposure.	YN	Individual
8	The companies that produce these chemicals must be held responsible and therefore find a need to develop alternatives to the use of these chemicals.	N<	CAW Local 195, Environment Committee, Windsor
9	What should be striven for is zero discharge of NDMA, one of the more potent carcinogens, we are exposed to as a result of industrial processes that externalize the cost of health risks upon the public.	N<	Centre for International Studies, Nova Scotia
10	Zero discharge is costly for industry but cost could be passed onto consumer to reflect true cost of product. Consumer could then reexamine the need for the product.	N<	Pesticide Action Group, Guelph
11	Any guidelines restricting an industry's operating costs are often violated.	N<	Individual

12	It is very difficult and expensive to reduce concentrations. The precursors to NDMA were removed in early 1990 and the company is still able to produce a product essential to the company's success. But the community has suffered considerably and the taxpayer has borne the entire burden of dealing with the contamination.	N<	Assuring Protection for Tomorrow's Environment, Elmira
13	Very difficult and expensive to reliably treat water for NDMA at such low concentrations.	N>	Individual
14	Drinking water quality criteria should take into account appropriate health and cost considerations.	N>	American Water Works Association, Ontario Section
15	Methods, cost of removal and economic aspects have not been investigated.	N>	Form letter from PUC (14X)
16	Provides estimates suggesting that we will be spending almost $200 million per death avoided.	N>	Individual
17	Unfair burden is placed on industry which may make it uncompetitive.	N>	Individual
18	Suggests that it makes more sense to ask the public to reduce the intake of some high NDMA foods rather than setting a low water standard which may have little or no basis in scientific assessment and which carries potentially serious economic consequences.	N>	Individual

APPROACH - MODEL USED			
	Comment	**Code**	**Respondent**
1	Agrees with use of BIBRA data and Weibull model.	Y	Hiram Walker & Sons, Windsor
2	Finds the proposed standard acceptable because: Hazard identification is based on more than 1 long term study, exposure assessment considers multiple routes of exposure, dose response assessment is extrapolated from 4 bioassay data sets which meet EPA criteria for technical accuracy of animal carcinogen studies.	Y	Rohm and Haas Canada, Inc., West Hill
3	Risk assessment framework is sound, hazard identification and exposure assessment phases are complete, tumour incidence data set and mathematical extrapolation model is suitable, assumptions used to characterize risk are appropriately conservative.	Y	Regional Municipality of Durham
4	Raise concerns about the high doses of NDMA administered in tests. Are also concerned about estimations of risk of cancer being extrapolated from the very high levels.	YN	PUC of the City of Brantford
5	Cites testimony of Dr. Lijinsky at the Environmental Appeal Board Hearing in the matter of Uniroyal as claiming that the only safe dose of NDMA is no dose at all.	N<	Assuring Protection for Tomorrow's Environment, Elmira
6	NDMA appears to be ubiquitous in the natural environment at 1 ppt. Is a dose-response function which intersects at (0,0) defensible?	N>	Blue Sky Research
7	Cites weakness of epidemiological data, suggests that use of conservative slope factors means that data need to be massaged, problem of biological response differences not considered.	N>	Individual
8	No doubt that NDMA is carcinogen at Maximum Tolerated Dose but no evidence at lower doses nor humans.	N>	Individual

9	Should use model in risk assessment that provides for endogenous production of NDMA.	N>	Individual
10	Model should be reassessed using linear multistage procedure which accounts for technological limitations and sampling error.	N>	Chemical Manufacturers Association, Washington, DC
11	Linear multistage model (which is normally the model of choice of the EPA) is the most appropriate for NDMA and shows a good fit to the BIBRA data. Cites weaknesses in the Weibull model and model-free extrapolation. Points out that if all the same assumptions are made about dose scaling, rat lifespan and which tumours to include, the linear multistage model is the most conservative of the three.	N>	CanTox Inc. and Uniroyal Chemical Ltd., Elmira

CONSIDERATION OF SYNERGISTIC EFFECTS			
	Comment	Code	Respondent
1	Suggests sensitizing local health units in affected areas especially in view of possible synergistic effects.	Y	Atwood Cheese Company, Atwood
2	There is no vehicle to address synergistic effects of combinations, suggests use of maximum total organic and maximum total inorganic as solution to this problem.	Y	CANVIRO, Waterloo
3	Not allow any traces of NDMA in water to allow for cumulative effects from other media and other chemicals.	N<	Z.I.P. Communication and Marketing, Cornwall
4	Does NDMA combine with other chemicals to create another hazardous chemical which will contribute to other diseases and conditions?	N<	Pesticide Action Group, Guelph
5	Concerned that synergistic effects of multitude of manmade contaminants are not fully understood.	N<	Individual

ENFORCEMENT			
	Comment	Code	Respondent
1	Expects that if the water were found with concentrations greater than 9 ppt then suspect supply would be shut off and an alternate supply found.	Y	Hiram Walker & Sons, Windsor
2	Assumes that standards will be strongly enforced.	Y	Individual
3	Concerned about the cost of enforcement.	YN	Individual
4	A much stricter process to ensure compliance must be adopted since guidelines are often violated and enforcement compromised due to inadequate funding, short staffing and inadequate intermittent sampling.	N<	Individual

OTHER AREAS TO INVESTIGATE			
	Comment	Code	Respondent
1	Look at exposure data from Germany, Finland and Sweden for soil.	Y	Paudash Lake Conservation Association
2	Studies on interaction of NDMA and soil should be explored as this is a pathway of large significance and should be understood.	Y	Great Lakes Environment Systems, Burlington
3	Should be consistent followup in areas where information is lacking, for example soil.	Y	Individual
4	Is there any evidence on effects on immature/growing systems? Are infants and children at greater risk?	Y	Wellington-Dufferin-Guelph Health Unit
5	Destiny of NDMA in the vegetation component is not mentioned, is this lack of significance or lack of knowledge?	YN	BC Environment

GENERAL PROCESS/FORMAT			
	Comment	**Code**	**Respondent**
1	Impressed with the speed with which the Committee has acted.	Y	Individual
2	Commends MOE on process with which to review material and the format adopted in outlining conclusions and considerations. Has presumptive faith in MOE's presentation of data.	Y	Individual
3	Questions if the right process is being used since NDMA has been found in only 1 place in Ontario and the source has agreed to clean up. Other sources should be controlled by Certificates of Approval.	Y	Individual
4	Hopes that this process will be used when other environmental standards are determined. Appreciates chance to comment, is not a scientist but understood the documentation. Public is interested and although not experts, have ideas to offer.	Y	Individual
5	Hopes that this process is followed when other environmental standards are determined.	Y	Regional Municipality of Durham
6	Is it adequate to protect only human health? What about effects on the environment and microorganisms? Limitations of the methodology will not be clear, suggest attaching a qualifier to each IMAC.	YN	B.C. Environment
7	Something that is limited to susceptible locations.	YN	Councillor, Township of Medonte, Barrie
8	Questions the priority given to NDMA. There are many other contaminants which are even more concerning.	YN	Rhone-Poulenc Canada Inc., Mississauga
9	Concern that "toxic" material is only worth a low level if it causes cancer. What about all the other effects chemicals can cause?	YN	Individual

10	Concern that a standard should protect any member of the public (including a child).	YN	International Institute of Concern for Public Health, Toronto
11	Relies on groups such as ACES to make decisions. Integrity and wisdom of a committee such as yours are the guides for the ordinary citizen.	YN	Individual
12	Concern that there was no dialogue with affected utilities nor review of the economic effects of implementation as is usually the case when changes to potable water are considered.	YN	Regional Municipality of Ottawa-Carlton
13	Recommend that rather than setting numbers a presence/absence approach be taken.	YN	Investigative Science Inc.and Six Nations Band Council
14	Knowledge gaps should be clearly identified and a clearer separation be made between fact and opinion.	YN	Individual
15	Very negative letter regarding waste of taxpayers' dollars on this type of process when the public does not know what NDMA is.	YN	Individual
16	We would hope that a value exempt from all limitation factors other than toxicity be clearly stated in all documentation in such a way as to identify those areas where development (analytical or technological) is needed.	YN	Ministry of the Environment, Quebec
17	More information should be provided on exactly what NDMA is and how the level will further affect the water.	N<	CAW Local 195 Environment Committee, Windsor
18	Should recommend 9 as MCLG only since risk management aspects such as routine monitoring capability and treatment technology have not been covered.	N>	American Water Works Association, Ontario Section
19	Population exposure and capability of monitoring on a routine basis have not been considered.	N>	Form letter from PUC (14X)

20	Objects to regulatory exercise of this nature since they are based on inadequate scientific knowledge and environmentalist dogma.	N>	Individual
21	Thorough survey needs to be done before any limit is set.	N>	Individual

Note: Respondents which believe in Zero Discharge could also be considered to disagree with the general process but are not listed in General Process

APPENDIX 2

LIST OF RESPONDENTS

R.G. Aldi - Manager, Quality Assurance and Environmental Compliance, Hiram Walker & Sons, Windsor

F.E. Bales - Director, Research and Development, Pylon Electronic Development Company Ltd., Nepean

A.F. Barton - Chair, Environment Committee, Consumers' Association of Canada (Ontario), Toronto

C.R. Bennet - Burlington

R. Bertell - International Institute of Concern for Public Health, Toronto

R.H. Boehnke - Etobicoke

M. Bokhout - Medical Officer of Health, Huron County Health Unit, Clinton

J.L. Boldt - Port Stanley PUC, Port Stanley

K. Bondy - Chairperson, C.A.W. Local 195 Environment Committee, Windsor

S.B. Bray - President, W.C. Investments Inc., Elmira

S. Bryant - Uniroyal Subcommittee of Assuring Protection for Tomorrow's Environment, Elmira

J.M. Buhlman - Barrister, Weir and Foulds, Toronto (for CanTox Inc.)

S. Cadeddu - Atwood Cheese Company Ltd., Atwood

E.E. Charters - Director, Corporate Safety, Health and Environment, CIBA-Geigy, Mississauga

P. Child - Principal, Investigative Science Incorporated and C. Montour - Director of Operations, Six Nations Council

M.G. Christie - Secretary/Manager, Greater Napanee Water Supply and Pollution Control Board, Napanee

T.J. Currah - Environmental Coordinator, Canadianoxy Chemicals, Fort Erie

N.H. Dalziel - Councillor, Township of Medonte, Barrie

R. Denham - Commissioner, Regional Municipality of Ottawa-Carlton, Environmental Services Department, Ottawa

L.E. Denys - General Manager, Wallaceburg Water Commission, Wallaceburg

K.A. Dickson - Water Department Supervisor, Brockville PUC, Brockville

G.P. Dunsmore - Elmira

P. Durand - Emsdale

G.L. Edwards - Owen Sound

K.L. Edwards - General Manager, Windsor Utilities Commission, Windsor

M. Emms - Water Works Superintendent, The Corporation of Township of Tiny Water Works Department, Perkinsfield

J. Farmer - Division Manager, Technical Services, RBW Graphics, Owen Sound

R. Ferris - Regional Manager, Dames & Moore Canada, Oshawa

M.G. Foster Roberts - Laboratory Manager, Zenon Environmental Laboratories, Burlington

N.L. Fraser - Nepean

I. Guay - Aquatic Toxicology Specialist, Toxic Discharge Assessment Department, Ministry of the Environment, Ste. Foy, Quebec

M. Hagerman - Stirling Public Utilities Commission, Stirling

H. J. Handke - Wella Canada, Oakville

P. Harrison - Special Projects Technician, Office of the Commissioner of Engineering, The Regional Municipality of York, Newmarket

D.G.W. Hartwell - General Manager, Lindsay Water Commission, Lindsay

J.R. Hase - Water Engineer, Kingston PUC, Kingston

P. Hegler - Commissioner of Work, Township of Bosanquet, Thedford

D. Hicks - Special Projects Officer, Manitoba Hydro, Winnipeg, Manitoba

R. Holme - Chair-Elect, American Water Works Association, Ontario Section, Toronto

H. Hoselton - Chairman, PUC of Cobourg, Cobourg

S. Houser - Etobicoke

F. Huber - Toronto

B. Humby - London

G. Hunnius - President, Paudash Lake Conservation Association, Toronto

B. Jantzi - Blue Sky Research, Oakville

A. Jones - Vice-President, Environmental Affairs, Rhone-Poulenc, Mississauga

A. Jones - Scarborough

M.J. Kern - Sarnia

D.C. Kittle - Medical Officer of Health, Wellington, Dufferin, Guelph Health Unit, Fergus

S. Kleinau - Secretary, Bruce Peninsula Environment Group, Lion's Head

J. Kollek - Dundas

R.J. Kyle - Medical Officer of Health, The Regional Municipality of Durham, Oshawa

R. Laughton - Pollutech Environmental Ltd., Oakville

J. MacFarlane - Chief Operator, Water/Wastewater Operations, Corporation of the Town of New Liskeard, New Liskeard

B. Mandryk - Operations Analyst, Great Lakes Environmental Systems Inc., Burlington

D.E. Manlow - Manager, Trenton P.U.C., Trenton

P. Maslak - London

G.D. McKenzie - Associate Professor of Geology, Ohio State University (summer resident of Ontario)

R. Mielke - Copper Cliff

G.N. Morrison - Elmira

P. Oltmann - Chromatography Group Leader, Manitoba Research Council, Portage la Prairie, Manitoba

N. Parrot - Norwood

R.J. Patrick - Director of Operations, PUC of the City of Brantford, Brantford

J. Popelas - Chairman, Kingsville PUC, Kingsville

J.A. Pursel - Waterloo

B.D. Robertson - Z.I.P. Communications and Marketing, Cornwall

A.E. Robinson - Toronto

J. Salter - Water Supervisor, Stratford PUC, Stratford

A. Schneider - Centre for International Studies, University College of Cape Breton, Sydney, Nova Scotia

D. Shanahan - Environment Manager, Rhone-Poulenc Canada Inc., Mississauga

S. Sikorski - Brampton

G.D. Strickland - Vice-President, Technical Services, Chemical Manufacturers Association, Washington, DC

D. Sutherland - Chief Chemist, CANVIRO Analytical Laboratories Ltd., Waterloo

M.G. Truscott - Dundas

J.W. van Barneveld - Integrated Management Branch, B.C. Environment, Victoria

J. VanBuskirk - Technical Control Supervisor, Scott Maritimes Ltd., New Glasgow, Nova Scotia

R.C. Vogan - Picton

B. Walter - Pesticide Action Group, Cambridge

V.J. Whalley - Occupational Health/Industrial Hygiene Coordinator, Rohm and Haas, West Hill

C. Woods - Pesticide Action Group, Guelph

P.R. Youakim - Technologist, Environment Canada, Burlington

APPENDIX 3

NDMA SAMPLING RESULTS

Ontario
Ministry of the Environment
Ministère de l'Environnement

Water Resources Branch

Water Resources Branch
125 Resources Road
Rexdale, Ontario
M9W 5L1

Direction des ressources en eau
125, chemin Resources
Rexdale (Ontario)
M9W 5L1

(416) 235-5822
FAX 235-6059

3 July 1991

MEMORANDUM

TO: Dr. K. Roberts
Manager
Drinking Water Section

FROM: R. B. Hunsinger
Supervisor
TA Unit

RE: NDMA Sampling Program

Heather Broomer from the Technology Assessment Unit has completed the NDMA survey of 30 water treatment plants in Ontario.

Enclosed, for your information, is a report summarizing the results of this survey. NDMAs were not detected in raw or treated water at any of the plants sampled.

The cooperation and help of John McGrachan (DWSP) was appreciated and essential to the completion of this study.

If you should have any questions regarding this report, please call Heather Broomer at 235-5824.

R. B. Hunsinger for
Ron Hunsinger

cc: B. Jobb
J. Dart
H. Graham
G. Jenkins
C. Sackville-Duyvelshoff
J. Smith

RBH/og

NDMA SAMPLING SURVEY OF ONTARIO DRINKING WATER TREATMENT PLANTS

Recent research concerning N-nitrosodimethylamines(NDMA), a known carcinogen has indicated that NDMA formation occurred when polyelectrolytes were used in conjunction with chlorine. It has been demonstrated that NDMA can be easily generated in pure water at room temperature if both chlorine and a polyelectrolyte of the polydiallyl dimethylamine type are present at 1% concentrations.[1] Since several water treatment plants in Ontario use both chlorine and polyelectrolytes the potential for NDMA formation exists.

As a result the MOE Water Resources Branch Drinking Water Section conducted a sampling program to address this concern. Sampling occurred from September 1990 to April 1991. All samples were submitted to the MOE Laboratory Services Branch (LSB) for NDMA analysis. Four samples per week were submitted for NDMA analyses. Thus, one raw and one treated water sample for two different plants were analyzed each week.

Preparation for the study involved locating water treatment plants with the greatest potential for NDMA formation. Three water treatment plants using the polydiallyl dimethylamine type polyelectrolytes were identified: Alvinston, Burlington and Thunder Bay(Bare Point). Further investigation indicated that Burlington only used the polyelectrolyte occasionally and it was not in use for the duration of this study. Consequently, Alvinston and Thunder Bay water treatment plants were sampled first.

Additional water treatment plants were selected according to their use of polyelectrolytes; other coagulants; other coagulant aids; or the raw water source. The results of the analyses are provided in the appended tables.

NDMA was not detected in any raw or treated water samples taken at any of the water treatment plants surveyed.

---

[1] REACTION BETWEEN CHLORINE AND A DIMETHYLAMINE CONTAINING POLYELECTROLYTE LEADING TO THE FORMATION OF N-NITROSO DIMETHYLAMINE, Pollutech Environmental Limited, Health and Welfare Canada & Environment Canada, 1990.

July 4, 1991

NDMA SAMPLING PROGRAM RESULTS

LOCATION	RAW WATER SOURCE	TREATMENT METHOD	COAGULANT AID	TYPE	SAMPLE	RESULT
ALVINSTON	Sydenham River	conventional with alum	KED CHEM 9010	PDD	raw	ND .005
					treated	ND .005
ARNPRIOR	Madawaska River	conventional with alum; chlorination	ALCHEM 8170	polyacrylamide	raw	ND .005
					treated	ND .005
ATIKOKAN	Atikokan River	direct filtration with alum; chlorination	CYNAMID N300	polyacrylamide	raw	ND .005
					treated	ND .005
BRANTFORD	Grand River	conventional with alum and PAC; prechlorination, chloramination	ACTIVATED SILICA		raw	ND .005
					treated	ND .005
BURLINGTON	Lake Ontario	direct filtration with alum; prechlorination	CATFLOC T SEASONAL	PDD	raw	NR
					treated	NR
CARLTON PLACE	Mississippi River	conventional; chlorination	PERCOL LT24	polyacrylamide	raw	ND .005
					treated	ND .005
CASSELMAN	South Nation River	conventional with alum; prechlorination; PAC added	PERCOL LT25	polyacrylamide	raw	ND .005
					treated	ND .005
CAYUGA	Grand River	conventional with polyaluminum chloride	ACTIVATED SILICA		raw	ND .005
					treated	ND .005
DESERONTO	Bay of Quinte	conventional with alum; prechlorination	AQUAFLOC 6465	polyacrylamide	raw	ND .005
					treated	ND .005
DRYDEN	Lake Wabigoon	conventional with alum	ALCHEM 8171 SC	polyacrylamide	raw	NR
					treated	NR
EMO	Rainy River	conventional; chlorination	ALCHEM 8170	polyacrylamide	raw	ND .005
					treated	ND .005
FRANKFORD	Trent River	direct filtration with alum; chlorination	NONE		raw	ND .005
					treated	ND .005
HASTINGS	Trent River	conventional with alum; chlorination	NONE		raw	ND .005
					treated	ND .005
HAWKESBURY	Ottawa River	conventional with alum; prechlorination	ACTIVATED SILICA		raw	ND .005
					treated	ND .005

PDD - polydiallyl dimethylamine; NR - no results; ND - not detected; IS - insufficient sample; * - higher detection limit

NDMA SAMPLING PROGRAM RESULTS CONT'D

LOCATION	RAW WATER SOURCE	TREATMENT METHOD	COAGULANT AID	TYPE	SAMPLE	RESULT
KENORA	Lake of the Woods	conventional with alum; prechlorination	PERCOL LT24	polyacrylamide	raw treated	ND .005 ND .005
LINDSAY	Scugog River	conventional with alum and activated silica; chlorination	A110 SUPERFLOC	polyacrylamide	raw treated	ND .010* ND .010*
LORNE PARK	Lake Ontario	conventional with alum; prechlorination	NONE		raw treated	ND .010* ND .010*
MITCHELL'S BAY	Lake St. Clair	conventional with alum; PAC added	PERCOL 727	polyacrylamide	raw treated	ND .005 ND .005
ODESSA	Millhaven Creek	conventional with alum; prechlorination	DEARBORN 6465	polyacrylamide	raw treated	ND .005 ND .005
PRESCOTT	St. Lawrence River	conventional; chlorination			raw treated	IS ND .005
RAINY RIVER	Rainy River	conventional; chlorination	ALCHEM 8170	polyacrylamide	raw treated	ND .005 ND .005
ROCKLAND	Ottawa River	conventional; chlorination	PERCOL LT25	polyacrylamide	raw treated	ND .005 ND .005
SUDBURY (Wanapitei)	Wanapitei River	direct filtration with alum; chlorination	PERCOL LT20	polyacrylamid	raw treated	ND .005 ND .005
TECUMSETH	grd source; Bond Head well supply	conventional; chlorination	ALCHEM 8171 SC	polyacrylamide	raw treated	ND .005 ND .005
TIMMINS	Mattagami River	conventional; chlorination	ALCHEM 8170	polyacrylamide	raw treated	ND .005 ND .005
THUNDER BAY (Bare Point)	Lake Superior	direct filtration with alum; prechlorination	PERCOL LT35	PDD	raw treated	ND .010* ND .010*
UNION	Lake Erie	conventional with alum; prechlorination, PAC used	ALCHEM 8171 SC	polyacrylamide	raw treated	ND .005 ND .005
WALPOLE ISLAND	St. Clair River	conventional with alum; prechlorination	ALCHEM 8170	polyacrylamide	raw treated	ND .005 ND .005
WINDSOR	Detroit River	conventional with alum; prechlorination	PERCOL LT24	polyacrylamide	raw treated	ND .005 ND .005

PDD = polydiallyl dimethylamine; NR = no results; ND = not detected; IS = insufficient sample; * = higher detection limit

APPENDIX 4

Models Used in NDMA Risk Assessments

The risk assessments of NDMA considered by ACES all used data derived from the British Industrial Biological Research Association (BIBRA) carcinogenicity bioassay. This bioassay, and indeed all bioassays like it, involve the administration of relatively high doses of a chemical to groups of experimental animals. These doses are generally far in excess of typical human exposure levels, but the higher doses are required to minimize the number of animals used. For example, if one were to try to administer a dose of carcinogen so low that the increased risk of developing cancer was one in one million, the number of animals required would be well in excess of one million. Obviously, the use of this many animals is not feasible. Therefore, the bioassays are designed to use higher doses and fewer animals. This necessitates the use of mathematical models to extrapolate from the high dose data to the lower range of human exposure doses. The goal of such models is to estimate the true relationship between lifetime exposure to a carcinogen and tumour incidence.

Depending upon the model chosen to extrapolate from the experimental dose range down to the low dose range, the shape of the dose-response curve can vary dramatically. There is no way for us to know how the dose-response curve actually looks in the low dose range, nor can we know whether the shape of the curve is the same for humans as for the animal species used in the bioassay. We must therefore rely on the best possible estimate, hoping that the calculated slope factor is conservative enough that it does not exceed the true slope factor. Three models which have been proposed for NDMA risk assessment are discussed below. All three of these models assume linearity of the dose-response curve in the low dose range.

One should keep in mind that the choice of extrapolation model is not the only factor affecting a risk assessment. Decisions must also be made about the most appropriate tumour data to incorporate, the appropriate dose scaling procedure to extrapolate from animals to humans, and the length of lifespan of the animals and humans, etc. These factors are not considered in the discussion below.

Weibull Model

The Weibull mathematical model can be used for bioassay data sets in which information about dose and length of time to tumour development is known. The model is linear at low doses, but it allows for the dose-response curve to flatten out at high doses. The Weibull model provides an estimate of cancer risk in the absence of competing risks.

A description of how the Weibull model was applied to the BIBRA data is provided in a paper by Peto *et al.* (IARC Scientific Publications (1984) No. 57, pp. 627-665). Briefly, a mathematical formula is used to summarize the distribution of time to occurrence of tumours. The model is a function of the number of years of treatment, the median time-to-tumour (which is dependent on the dose rate), and the probability of death due to tumour.

The Weibull model assumes that cancer originates in a single cell and that the individual cells in a given tissue behave independently. However, these assumptions can never be verified. Also, the physiological interpretation of this model is not clear at the present time.

The primary advantage of the Weibull model in NDMA risk assessment is that the BIBRA study was designed to be assessed using a time-to-tumour model. Therefore, the Weibull model makes efficient use of the BIBRA study data. It has also been found to fit the observed data well.

However, the model has been criticized since time-to-tumour data relies heavily on palpation of tumours (examination of the rats by touching or feeling for tumours) to assess when tumours develop. Such an assessment may be unreliable.

Another criticism of the model (as used by Peto *et al.*) is that the data for the lowest four dose groups, which were pooled together for the sake of statistical stability, should have been considered individually in order to make better use of data in the low dose range.

The Weibull model was chosen as the most appropriate risk assessment model for NDMA by the U.S. EPA.

Linearized Multi-Stage Model

The linearized multi-stage model involves first trying to fit a line to the dose-response data for all doses. If this line does not have an acceptable fit (as determined statistically by the computer program ToxRisk), then the highest dose is

omitted and a line is re-fit to the remaining data. This procedure continues until the first line having an acceptable fit using the greatest amount of data is found. The upper 95% confidence limit of the slope of this line is usually the value used for risk assessment purposes.

This mathematical model is the one that is normally used and endorsed by the U.S. EPA for risk assessment purposes, unless another model can be shown to be more appropriate for a given data set. In the case of NDMA, the U.S. EPA evidently felt that the Weibull model, as applied by Peto *et al.*, was more suitable for the data observed in the BIBRA study.

The linearized multi-stage model estimates the risk of cancer in the presence of competing risks. The model makes certain assumptions which have a basis in physiology. For example, the model assumes that cancer is initiated in a single cell and progresses through a discrete number of biological stages. The model also assumes that the rate of cancer development is constant within each of these biological stages and that the rates are related to the dose of carcinogen. However, these assumptions can never actually be verified.

An advantage of this model is that it provides an adequate fit to data obtained from many different bioassays. Although the model does not fit data that flattens out at high doses, the data in the high dose region can be eliminated until the model does provide a good fit (as described above). For risk assessment purposes, the high dose data is considered to be less relevant than the trend for low dose data since human exposure is generally in the low dose region. Tumour incidence in experimental animals is sometimes observed to "flatten out" at high doses due to premature death (as a result of the chemical's toxicity at high doses causing death before the animals have a chance to develop cancer) or due to saturation of the metabolic pathways in the animals (i.e. the rate of metabolic activation of chemicals to their active, carcinogenic form becomes a limiting factor for tumour development).

Model-Free Extrapolation (Linear Robust Model)

The model-free extrapolation fits a straight line between two points. The first point is determined by finding the lowest dose which gives a response that is statistically significantly different from the response in control animals. The upper 95% confidence limit of the response one dose below this is used as the first point on the line. The second point is the lower 95% confidence limit of the response observed in animals receiving the control dose (zero dose). If the lowest dose used produces a response that is significantly greater than

the response in controls, then this is the dose used in the linear extrapolation.

This approach to risk assessment was developed by D. Krewski of Health & Welfare Canada and is described in an article by Krewski *et al.* (Environmental Health Perspectives (1991) Vol. 90, pp. 279-285). In this article, slope factors determined using the model-free approach are compared with those determined for the same data using the linearized multi-stage model. The median ratio of slope factors (model-free/multi-stage) obtained is 1.3, indicating that the model-free approach tends to produce somewhat higher slope estimates than the linearized multi-stage model.

An advantage of the model-free extrapolation is that it makes no assumptions about the physiological processes involved in cancer development. The only assumption made in this approach is that at low doses, the dose-response curve is linear (or sublinear, in which case the calculated slope factor will be an over-estimate of the true slope).

The disadvantages of this extrapolation procedure are that it makes inefficient use of the data (since only two data points are used), and its validity has not been properly assessed (since it has not yet been used much in practice, nor has it been subjected to extensive peer-review).

Further Reading

Crump, K. Comments on a model-free extrapolation (MFX) approach. In: *Biological Risk Assessment of N-Nitrosodimethylamine (NDMA)*. CanTox Inc. (1990).

Crump, K.S. Comments on the cancer potency estimates for N-nitrosodimethylamine made by the U.S. Environmental Protection Agency. In: *Biological Risk Assessment of N-Nitrosodimethylamine (NDMA)*. CanTox Inc. (1990).

Krewski, D., Gaylor, D. and Szyszkowicz, M. A model-free approach to low-dose extrapolation. Env. Health Perspect. 90:279-285 (1991).

Peto, R., Gray, R., Brantom, P. and Grasso, P. Nitrosamine carcinogenesis in 5120 rodents: chronic administration of sixteen different concentrations of NDEA, NDMA, NPYR and NPIP in the water of 4440 inbred rats, with parallel studies on NDEA alone of the effect of age of starting (3, 6 or 20 weeks) and of species (rats, mice or hamsters). In: *N-Nitroso Compounds: Occurrence, Biological Effects and Relevance to Human Cancer*. IARC Sci. Publ. No. 57:627-665 (1984).

APPENDIX 5

TESTIMONY RELEVANT TO STANDARD-SETTING FOR NDMA

(from the Environmental Appeal Board Hearing of the appeal by Uniroyal Chemical Ltd. of a control order under s.32(1) and s.8 of the Ontario Water Resources Act - File SWA.011.90, SWA.013.90, SWA.014.90)

Preamble

This document was prepared by an independent researcher hired by the Advisory Committee on Environmental Standards. The document is intended to provide a summary of the relevant toxicological and risk assessment information about N-nitrosodimethylamine (NDMA) recorded in the transcripts of testimony heard by the Environmental Appeal Board. A comparison of the results of risk assessments by several agencies is included. This comparison provides a synthesis and some interpretation of information from the hearing and agency risk assessment documents.

General Notes Extracted from Testimony

- NDMA is classified as a probable human carcinogen, based on the weight of evidence from animal studies (IARC, U.S. EPA, OSHA).

- NDMA has been shown to produce cancer in about 40 species.

- Ontario Ministry of Labour has not established any exposure values for NDMA, although they call it a "known toxic agent...to which any exposure should be avoided", since direct or airborne contact "may result in significant absorption...through the skin, mucous membranes or eyes".

- NDMA is decomposed by exposure to ultraviolet light, but special measures must be taken to prevent the breakdown products from re-combining. One possible measure is the addition of peroxide, but this may result in the formation of other carcinogens which are less potent, but more stable than NDMA.

- NDMA does not bioaccumulate, but its carcinogenic effects are cumulative.

- In vitro studies appear to show that NDMA metabolism is similar in both human and animal tissues.

- British Industrial Biological Research Association (BIBRA) NDMA bioassay did not use infant or weanling rats, although these are probably more sensitive to toxic effects.

- Tumour development (carcinogenesis) is a more sensitive endpoint than either fetotoxicity or teratogenicity in NDMA bioassays.

- Health & Welfare Canada (HWC) recommended that "concentrations of NDMA in drinking water be minimized to the extent possible and that levels not exceed the limit of detection of the analytical method currently being used by the [Ontario] Ministry [of the Environment] (i.e. <10 ng/L)".

A COMPARISON OF NDMA RISK ASSESSMENTS
BASED ON TESTIMONY PROVIDED MAINLY BY DR. NESTMANN
AT THE ENVIRONMENTAL APPEAL BOARD HEARING

	MOE/Peto	EPA/Peto/ Brecher/ Waterloo Region	CanTox/ Nestmann/ Thomson/ Uniroyal	HWC
Bioassay	BIBRA	BIBRA	BIBRA	BIBRA
Model	Weibull	Weibull	Linearized multi-stage*	Linear robust
Rats/Tumours Used	F only; all tumours	F only; all tumours	Mean of M & F of specific tumour types*	M only; all tumours
Hyperplastic Nodules Included?	No	No	No	Yes
Rat Lifespan	3 years	3 years	2 years*	2 years ?
Dose Scaling Factor	6.5	6.5	1*	6.5
Water Consumption	1.5 L	2.0 L	1.5 L	1.5 L
Risk Level	10^{-5}	10^{-6}	10^{-5}	10^{-6}
Peer Review	Based on EPA	Extensive	None	Inadequate?
Proposed NDMA Level	9 ppt	0.68 ppt	205.6 ppt	0.04 ppt

Notes on Abbreviations:

Dr. Earle R. Nestmann, Ph.D. (witness called by Uniroyal Chemical Ltd.) is the Senior Scientist in Toxicology for CanTox Inc.

*Dr. **Mark Thomson**, Ph.D. (witness called by Uniroyal Chemical Ltd.) is a corporate toxicologist for Uniroyal Chemical Co. Inc. in Middlebury, CT. He concurred with Dr. Nestmann on the points indicated by an asterisk. Dr. Thomson's testimony does not appear to have addressed the other matters relating to the NDMA risk assessment.

Dr. Ronald Brecher, Ph.D. (witness called by the Regional Municipality of Waterloo) is head of the Human Health Assessment Division for EcoLogic.

MOE = Ontario Ministry of the Environment
EPA = U.S. Environmental Protection Agency
HWC = Health & Welfare Canada
BIBRA = British Industrial Biological Research Association
ppt = parts per trillion

Choice of Bioassay

All four groups agreed that the BIBRA study was the most appropriate to use for NDMA risk assessment, due to the study's design and large sample size.

Choice of Dose-Response Extrapolation Model

- The linearized **multi-stage model** (which is generally used by the EPA unless there is evidence that another model is more appropriate) was criticized for: 1) its lack of fit to data that flattens out at high doses; 2) its use of an arbitrary polynomial exponent that represents the number of stages leading to cancer development; 3) its insensitivity to the shape of the dose-response curve in the observable range; and 4) its instability and variability over about two orders of magnitude, depending on the number of exponents used. Therefore, the multi-stage model may not adequately represent the biological processes at work in NDMA carcinogenesis.

- The **Weibull time-to-tumour model** appears to fit the BIBRA data better since it allows for a supralinear dose-response curve (i.e. one that flattens out at high doses). It also incorporates all the BIBRA data (dose and time-to-tumour). A drawback of the Weibull model is that one of the critical parameters in the dose-response function "has no apparent physiological interpretation at present".

- HWC used the **linear robust model** (also known as the model-free approach) in their risk assessment since they felt the time-to-tumour model of Peto *et al.* relied too heavily on palpation to determine when animals developed tumours. The linear robust model uses few assumptions about the physiological processes involved in cancer development. A disadvantage of this model is that is has not been used enough for its validity to be properly assessed.

Choice of Rats/Tumours Used

Dr. Nestmann of CanTox derived a separate slope factor for each specific tumour type recorded in the BIBRA data for which there was a statistically significant dose-response relationship. He then took the highest slope factor for females (which was for biliary cystadenomas) and the highest for males (hepatocellular adenomas + carcinomas) and averaged them. This was his final slope factor which he used throughout the rest of his risk assessment report. The rest of the BIBRA tumour incidence data was not used in the subsequent stages of his risk assessment. Dr. Nestmann and Dr. Thomson both believe it is inappropriate to combine tumour types unless they are histogenically related. For

example, hepatocellular adenomas and hepatocellular carcinomas may be combined, since they arise from the same cell type. However, hepatocellular tumours should not be combined with tumours such as biliary cystadenomas.

Dr. Brecher of EcoLogic felt that "the incidence of all types of tumours should be considered since...the precise mechanism of carcinogenesis is unclear and because the type, location and incidence of tumours vary with species, route and modifying factors". In his opinion, a more "cautious approach" for the BIBRA data would be to combine all the liver tumour incidence data to derive a dose-response curve and slope factor.

Peto *et al.* used female tumour incidence data only since female rats appeared to be more sensitive to NDMA than males. HWC used male rats since their tumour incidence was higher in the lower dose groups. However, since the time of the Appeal Board hearing (May 1990), HWC appears to have re-evaluated its NDMA risk assessment and decided to use female tumour incidence data instead (refer to p. 44, Scientific Criteria Document for Multimedia Standard Development No. 01-90 N-Nitrosodimethylamine, March 1991).

All four groups included both benign and malignant tumours since there was no evidence to indicate that benign tumours would not progress to the malignant stage.

Inclusion vs. Exclusion of Hyperplastic Nodules

Both Dr. Nestmann and Dr. Brecher agree that hyperplastic nodules should be excluded from the tumour incidence data since no direct link has been shown between nodules and cancer, and the nodules are not life-threatening.

HWC apparently included hyperplastic nodules in their risk assessment which was current at the time of the Appeal Board hearing (May 1990). However, in their re-evaluation of their assessment they decided to exclude these nodules.

Length of Rat Lifespan

The longest mean rat lifespan for a dose group in the BIBRA study was 966 days, or between 2.6 and 2.7 years. The control male and female mean lifespans were 920 and 837 days (2.52 and 2.29 years), respectively. However, many rats in the high dose groups died within less than one year. In the highest dose group, male rats had a mean lifespan of 222 days, while female rats lived an average of 191 days. Toxicologists usually take the average lifespan of a rat to be 2 years, even though some rats have shorter and others have longer lifespans.

Choice of Dose Scaling Procedure

Dr. Nestmann feels that a body surface area correction should only be used when a chemical's metabolism is linked to basal metabolism. He argues that since NDMA is metabolised by the cytochrome P-450 system (which is not linked to basal metabolism), the body surface area correction is not appropriate for NDMA.

Dr. Brecher feels that since NDMA carcinogenesis probably involves other stages besides the biotransformation of NDMA by P-450, the scientific community "cannot state with any confidence that the process is not linked to basal metabolism". He therefore feels that the surface area correction is valid.

HWC used the surface area correction in their risk assessment, although they felt that not using it could also be justified.

Water Consumption Level

Based on a HWC survey, up to 16% of Canadians consume more than 2 L of drinking water per day. For this reason, Dr. Brecher favours the use of 2 L/day for risk assessment purposes.

It should be noted that approximately 7% of Canadians aged 6-17 and 9% of Canadians aged 18 and over consume in excess of 2.5 L of drinking water per day. In these same age groups, 1.6% and 2.0%, respectively, consume more than 3.9 L/day.

Choice of Risk Level

Dr. Brecher argues in favour of a risk level of one in one million (10^{-6}) using the following logic: "If you have many sources and you desire a total risk that does not exceed one in 100,000 [10^{-5}], then each one of those sources must be regulated such that the risk is less than 10^{-5}."

Dr. Nestmann feels that the use of a 10^{-6} risk level is overly conservative.

Extent of Peer Review

Although the multi-stage model used by CanTox has been extensively peer-reviewed, the CanTox NDMA risk assessment report itself has not been subjected to any peer review. It is therefore not clear whether their use of the multi-stage model for the NDMA data is valid.

The use of the Weibull model by Peto *et al.* has undergone considerable peer-review.

As mentioned under the heading "Choice of Model", the linear robust model used by HWC has not been adequately peer-reviewed. However, HWC almost certainly had a group of experts review their assessment prior to release to the public.

EFFECT OF USING DIFFERENT ASSUMPTIONS ON THE NDMA LEVELS PROPOSED BY VARIOUS RISK ASSESSMENTS
(An analysis based on testimony provided mainly by Dr. Nestmann.)

	MOE	EPA	CanTox	HWC
Slope Factor for Rats	7.8/mg/kg/day	7.8/mg/kg/day	2.2699/mg/kg /day	180/mg/kg/ day
Proposed NDMA Level	9	0.68	205.6	0.04
10^{-6} Risk Factor	0.9[a]	0.68	20.56[a]	0.04
2 L Drinking Water/Day	6.8[b]	0.68	154.6[b]	0.03[b]
Dose Scaling Factor (rats→humans)	9	0.68	31.6[c]	0.04
Total Tumour Incidence, Excluding Nodules	9	0.68	128.5[d]	0.82[e]
2 Year Rat Lifespan	155.6[f]	11.6[f]	205.6	0.04
Cumulative Effect of All Assumptions Above	11.6	11.6	1.48	0.62

N.B. Unless otherwise stated, all values are given in units of parts per trillion (ppt) (equivalent to ng/L). The bottom row represents the final values of NDMA drinking water levels if all of the tabulated assumptions are used. These assumptions are described in greater detail below:

i) Risk level of 10^{-6}.
ii) Average drinking water consumption of 2 L/day.
iii) Surface area scaling factor of 6.5 is used (cube root of the ratio of average human weight (70 kg) to average rat weight (250 g)).
iv) Total tumour incidence is used, excluding hyperplastic nodules.
v) The standard rat lifetime of 2 years is used.

Footnotes Explaining Calculations:

[a] MOE and CanTox selected a risk level of 10^{-5}, so to convert to 10^{-6} risk level, divide by 10.

$$9/10 = 0.9$$
$$205.6/10 = 20.56$$

[b] To convert from assumption of 1.5 L water/day to 2.0 L, divide by 1.33 (=2 L/1.5 L).

$$9/1.33 = 6.8$$
$$205.6/1.33 = 154.6$$
$$0.04/1.33 = 0.03$$

[c] CanTox did not use the dose scaling factor used by the other risk assessors in extrapolating their slope factor from rats to humans. If they were to use the same dose scaling factor as the other risk assessors, their slope factor would be multiplied by 6.5, so NDMA level would be divided by 6.5.

$$205.6/6.5 = 31.6$$

[d] If CanTox were to use total tumour incidence, their slope factor would be 1.6 times greater (according to Dr. Nestmann), so NDMA level must be divided by 1.6.

$$205.6/1.6 = 128.5$$

[e] If HWC were to exclude hyperplastic nodules, NDMA level would increase by 20.55 times (see p.4061 of Dr. Nestmann's testimony).

$$0.04 \times 20.55 = 0.82$$

[f] If the MOE and EPA were to use a rat lifespan of 2 years instead of 3 in their model, their slope factor would be 17 times lower (according to Kenny Crump in the CanTox report), so the calculated NDMA level would be different.

The factor of 17 comes from the fact that the Peto *et al.* model used by the EPA and MOE includes the term t^7 (where t = time of rat lifespan in years). In order to convert the Peto *et al.* slope factor of 51/mg/kg/day, which corresponds to a 3 year rat lifetime, to the appropriate value corresponding to a standard 2 year lifetime, the following ratio can be established:

$$\frac{51}{3^7} = \frac{y}{2^7}$$

where y = the slope factor corresponding to an assumption of a 2 year lifespan for rats. Solving for y,

$$y = 51 \times 2^7/3^7$$

$$\doteq 51 \times 1/17$$

$$= 3/\text{mg/kg/day}$$

Substituting this slope factor into the formula to calculate the corresponding NDMA level:

$$\text{NDMA level} = \frac{\text{body weight x risk level}}{\text{water intake x slope factor}}$$

Using the MOE assumptions about risk level (10^{-5}) and water intake (1.5 L),

$$\text{NDMA level} = \frac{70 \text{ kg} \times 10^{-5}}{1.5 \text{ L} \times 3/\text{mg/kg/day}}$$

$$= 155.6 \times 10^{-6} \text{ mg/L}$$

$$= 155.6 \text{ ng/L or ppt}$$

Using the EPA assumptions about risk level (10^{-6}) and water intake (2 L),

$$\text{NDMA level} = \frac{70 \text{ kg} \times 10^{-6}}{2 \text{ L} \times 3/\text{mg/kg/day}}$$

$$= 11.6 \times 10^{-6} \text{ mg/L}$$

$$= 11.6 \text{ ng/L or ppt}$$

Summary

Since the MOE and EPA use the same extrapolation model (i.e. the Weibull model, as described by Peto *et al.*), it stands to reason that if they were to make all of the same assumptions, their proposed NDMA levels would be equal. The bottom row of the table above shows this to be true, since both agencies end up with an NDMA level of 11.6 ppt. The NDMA level of 205.6 ppt that was proposed by CanTox is dramatically reduced to 1.48 ppt when all of the factors corresponding to the different assumptions are applied in combination. The HWC's proposed NDMA level increases from 0.04 ppt to 0.62 ppt if the assumptions are modified to comply with those set out in the table.

APPENDIX 6

SUMMARY OF NDMA GUIDELINES IN OTHER JURISDICTIONS

(Modified from Ontario Ministry of the Environment (1991a, pg. 49)

Jurisdiction	Air (ng/m^3)	Water (ng/L)	Associated Risk Level	Comments	Reference
U.S. EPA	-	1.4[a]	10^{-6}	ambient water quality criteria: water and fish consumption	EPA, 1991
Minnesota	-	14	-	acceptable drinking water concentration	ATSDR, 1989
U.S. EPA	-	16,000[a]	10^{-6}	ambient water quality criteria: fish consumption only	EPA, 1991
Kansas	0.07	1.4	10^{-6}	acceptable drinking water concentration: annual average	ATSDR, 1989
Philadelphia	1.2	-	TLV-based	ambient air concentration: annual average	ATSDR, 1989
North Carolina	50	-	10^{-5}	ambient air concentration: annual average	ATSDR, 1989
Virginia	3000	-	TLV-based	ambient air concentration: 24 hour average	ATSDR, 1989

[a]The ambient water quality criteria remain as indicated; however, the human health criteria were adjusted based on cancer potency factor (03/01/88) and are as follows:
- 0.7 ng/L at 10^{-6} risk level for water and fish consumption
- 8000 ng/L at 10^{-6} risk level for fish consumption only.

REFERENCES CITED:

Agency for Toxic Substances and Disease Registry (ATSDR). 1989. Toxicological Profile for N-nitrosodimethylamine. Prepared by Syracuse Research Corporation for ATSDR in collaboration with U.S. EPA. United States Public Health Service.

U.S. Environmental Protection Agency. 1991. Integrated Risk Information System (IRIS). Risk Estimate for Carcinogenicity for N-Nitrosodimethylamine. On line. (Verification date 03/01/88). Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati Ohio.

APPENDIX 7

BACKGROUND MATERIAL ON NDMA

THE ADVISORY COMMITTEE ON ENVIRONMENTAL STANDARDS IS INTERESTED IN YOUR COMMENTS ON

NDMA

The Minister of the Environment has requested that the Advisory Committee on Environmental Standards review the documentation and obtain public input on the proposed new interim provincial drinking water guideline of 9 parts per trillion (ng/L) for the chemical N-nitrosodimethylamine (NDMA).

The Advisory Committee on Environmental Standards was established to contribute to environmental improvement by advising the Minister on standards for environmental contaminants. To ensure that these recommendations also reflect society's interests, we are seeking public input before reporting to the Minister and would like to invite you to take part in this public consultation.

We would like to know the public views on the suggested level, specifically with respect to the following:

1. Is the proposed standard acceptable?
2. If not, what is the basis for your finding the proposed level unacceptable?
3. Do you have an alternative level to propose?

Written comments will be accepted until November 27, 1991.

If you are concerned about the environment and would like to make a difference then get involved!

For further information, and copies of the documentation, please contact:

Advisory Committee on Environmental Standards
Ontario Ministry of the Environment
135 St. Clair Ave. West
Toronto, Ontario M4V 1P5
(416) 323-5034
(416) 323-5080 (fax)

Environment
Environnement

CCNE

LE COMITÉ CONSULTATIF SUR LES NORMES ENVIRONNEMENTALES SOLLICITE VOS COMMENTAIRES SUR LA

NDMA

La ministre de l'Environnement a demandé au Comité de revoir les documents portant sur la norme provinciale proposée pour la N-nitrosodiméthylamine (NDMA) dans l'eau potable, soit 9 parties par billion (10^{12}) (ng/L). Le Comité doit ensuite obtenir les commentaires du public à ce sujet, puis présenter ses recommandations.

Le Comité consultatif sur les normes environnementales a pour mandat de contribuer à l'amélioration de la qualité du milieu naturel; à cette fin, il présente au ministre de l'Environnement des recommandations pour l'établissement de normes en matière de polluants. Le Comité tient également à refléter les intérêts de la société. Aussi veut-il connaître l'opinion du public avant de présenter ses recommandations à la ministre. Il vous invite donc à participer à la consultation.

Les membres du Comité aimeraient connaître votre point de vue au sujet de la nouvelle norme, particulièrement sur les questions suivantes:

1. Est-ce que la norme proposée est acceptable?
2. Sinon, en quoi est-elle inacceptable?
3. Quelle norme proposeriez-vous?

Prière de faire parvenir vos commentaires avant le 27 Novembre , 1991.

Si vous souciez de la qualité de l'environnement et que vous aimeriez faire quelque chose, participez à cette consultation.

Pour obtenir plus de renseignements ou d'autres exemplaires du document, adressez-vous au :

Comité consultatif sur les normes environnementales
Ministere de l'Environnement
135, avenue St. Clair ouest
Toronto (Ontario) M4V 1P5
(416) 323-5034
(416) 323-5080 (télécopieur)

Ontario Environment Environnement

ENVIRONMENT
INFORMATION-
ENVIRONNEMENT

SUMMER 1991 — Environment Environnement — ÉTÉ 1991

PUBLIC REVIEW OF NEW DRINKING WATER GUIDELINE FOR NDMA

The minister has referred the Expert Committee Report and Ministry rationale for the 9ppt Interim Maximum Acceptable Concentration (IMAC) to Ontario's Advisory Committee on Environmental Standards to consult with the public and recommend a final Maximum Acceptable Concentration (MAC).

WHAT IS NDMA?

NDMA (N-Nitrosodimethylamine) is a chemical compound known to cause cancer in a wide variety of animal species, and may cause cancer in humans.

An odorless, tasteless, yellow, oily liquid at room temperature, NDMA is no longer produced for commercial purposes. However, it is an inadvertent byproduct of the chemical processes used in some industries such as rubber manufacturing, leather tanning, pesticide manufacturing and food processing, and as a result may be found in sewage treatment plant effluent.

OCCURRENCE IN ONTARIO

In November, 1989, the Ministry's Drinking Water Surveillance Program (DWSP) detected the first high concentration of NDMA in drinking water in Ontario at

EXAMEN PUBLIC DU NOUVEAU CRITÈRE DE QUALITÉ DE L'EAU POTABLE POUR LA NDMA

La ministre a transmis le rapport du comité d'experts et la justification du seuil de 9 ppt au Comité consultatif des normes environnementales de l'Ontario qui sollicitera l'avis du public et recommandera une concentration maximale admissible (CMA).

QU'EST-CE QUE LA N-NITROSODIMÉTHYLAMINE (NDMA)?

La N-nitrosodiméthylamine est un composé chimique dont on connaît le pouvoir cancérogène chez une grande variété d'espèces animales; ce composé pourrait même être une cause de cancer chez les humains.

Liquide jaune inodore, insipide et huileux à la température de la pièce, la N-nitrosodiméthylamine n'est plus fabriquée à des fins commerciales. Elle reste cependant un dérivé insidieux des procédés chimiques utilisés dans certaines industries, notamment celles du caoutchouc, du tannage du cuir, de la fabrication de pesticides et de la transformation des aliments. On en retrouve donc dans les effluents des usines d'épuration des eaux d'égout.

Elmira. No NDMA was detected in similar DWSP studies at over 40 locations across Ontario.

An Interim Maximum Acceptable Concentration (IMAC) of 14 ppt (parts per trillion) was adopted by the Ministry to reduce NDMA discharges and issue a control order to Uniroyal Limited -- making Ontario the first province in Canada to adopt such a guideline. The 14 ppt IMAC, based on readily available NDMA information, was a temporary measure taken to reduce discharges until a more in-depth analysis could be conducted.

The Ministry has continued monitoring drinking water supplies in the Grand River System serving Waterloo, Kitchener, Brantford and smaller communities along the river which empties into Lake Erie near Dunnville.

INTERIM MAXIMUM ACCEPTABLE CONCENTRATION (IMAC)

IMAC is a term used to describe limits for substances of concern with known chronic effects in humans and animals and for which there are no established maximum acceptable concentrations. When a substance is detected above the IMAC level, it signals the need for more sampling, investigation and corrective action on a case-by-case basis.

EXPERT COMMITTEE REVIEWS NDMA EXPOSURE\RISK

An Expert Committee was established by the Ministry in May, 1990, to identify potential guideline numbers and associated risk levels based on health considerations. All pathways of exposure to NDMA - via air, water, soil, diet and consumer products - were evaluated.

The health risk of NDMA exposure at various levels over a lifetime (incremental lifetime cancer risk) was assessed.

The Expert Committee included representatives from the Ministries of Environment, Health and Labour, and the Regional Municipality of Waterloo. Its report has assisted the Ministry in selecting a more appropriate IMAC for drinking water.

INCIDENCE EN ONTARIO

C'est en novembre 1989, à Elmira, qu'on a décelé, dans le cadre du Programme de surveillance de la qualité de l'eau potable du Ministère, la première concentration élevée de NDMA dans l'eau potable de la province. Aucune autre trace de NDMA n'a été relevée lors d'enquêtes menées dans plus de 40 localités de la province dans le cadre du même programme.

Le ministère de l'Environnement a adopté une concentration maximale admissible provisoire (CMAP) de 14 parties par billion (ppt) dans le but de réduire les rejets de NDMA et de délivrer un arrêté d'intervention à la société Uniroyal Limited, ce qui fait de l'Ontario la première province canadienne à adopter une telle directive. La CMPA de 14 ppt, fondée sur les données existantes concernant la NDMA, représentait une mesure provisoire visant à réduire les rejets jusqu'à ce qu'une analyse plus approfondie soit effectuée.

Le Ministère a continué de surveiller les sources d'approvisionnement en eau du réseau de la rivière Grand qui dessert Waterloo, Kitchener, Brantford et les plus petites localités longeant la rivière qui se jette dans le lac Érié, près de Dunnville.

CONCENTRATION MAXIMALE ADMISSIBLE PROVISOIRE (CMAP)

La CMAP décrit les seuils d'une substance préoccupante dont on connaît les effets chroniques sur les humains et sur les animaux et pour laquelle aucune concentration maximale admissible n'a encore été établie. La présence d'une substance à une concentration supérieure à la CMAP indique qu'il est nécessaire d'effectuer d'autres échantillonnages et d'autres enquêtes, et de mettre en oeuvre de nouvelles mesures correctrices adaptées à chaque cas.

UN COMITÉ D'EXPERTS ÉTUDIE LE RISQUE QUE PRÉSENTE L'EXPOSITION ¨ LA NDMA

En mai 1990, le Ministère a créé un comité d'experts chargé d'établir les seuils de NDMA admissibles et les risques qu'elle présente pour la santé. Toutes les voies d'exposition à la NDMA ont été évaluées, à

NEW NDMA DRINKING WATER GUIDELINE

A more stringent guideline (IMAC) for NDMA of 9 ppt in drinking water has now been adopted by the Ministry. This was based on the assessment of risks to health and relevant risk management factors such as analytical detection limits and relative risks from other sources of exposure.

The 9 ppt IMAC for NDMA represents an incremental lifetime cancer risk of 1 in 100,000. This is considered by regulatory agencies to be within the range of negligible risk. It is also a concentration which is analytically measurable.

The new IMAC for NDMA will be used to assess both drinking water and point source discharges and, where necessary, to control these discharges from sewage treatment plants and direct industrial dischargers.

savoir l'eau, le sol, l'alimentation et les biens de consommation.

On a aussi mesuré le risque progressif de cancer que présente l'exposition à la NDMA à différentes concentrations tout au long de la vie.

Le comité d'experts réunit des représentants des ministères de l'Environnement, de la Santé et du Travail, ainsi que de la municipalité régionale de Waterloo. Son rapport a aidé le Ministère à établir les concentrations maximales admissibles provisoires dans l'eau potable.

NOUVELLE LIMITE POUR LA NDMA DANS L'EAU POTABLE

Le Ministère a fixé une limite plus rigoureuse pour la NDMA dans l'eau potable. Cette nouvelle limite de 9 ppt est fondée sur l'évaluation du risque pour la santé et des facteurs pertinents de gestion des risques, tels les seuils de détection analytique et les risques relatifs inhérents à d'autres sources d'exposition.

La concentration maximale admissible provisoire, qui est fixée à 9 ppt pour la NDMA, représente un risque de cancer progressif de 1 sur 100 000. Selon les organismes de réglementation, cette concentration constitue un risque négligeable. Elle est par ailleurs mesurable en analyse.

La nouvelle concentration maximale admissible provisoire servira à évaluer la qualité de l'eau potable et des rejets de sources ponctuelles et, s'il y a lieu, elle permettra de contrôler les rejets des usines d'épuration des eaux d'égout et les rejets industriels directs.

PIBS 1623b
08/91 6M

ACES Members

Mark Goldberg*
Chair of ACES
Toxicology
University of Guelph
Guelph

Beth Savan
Vice Chair of ACES
Environmental Researcher and Educator
University of Toronto
Toronto

Robert Boldt
Occupational Health and Environment
Sarnia

Doug Cook
Occupational Health and Environment
Taurscale Consultants Ltd.
Toronto

Mary Morison
Occupational Health and Safety
Ontario Federation of Labour
Toronto

David Pengelly
Air Pollution Epidemiology
McMaster University
Hamilton

Ralph Stanley*
Public Health Protection
Peel Regional Health Department
Brampton

Keith Winterhalder*
Plant and Soil Ecology
Laurentian University
Sudbury

Ian Brindle*
Analytical Chemistry
Brock University
St. Catharines

Helen Henrikson
Physiology and Environmental Planning
Kingston

Sally Paterson*
Environmental Chemodynamics
University of Toronto
Toronto

Catherina Spoel
Environmental Law
Miller Thomson
Toronto

Peter Victor*
(resigned November 1991)
Environmental Economics
VHB Research and Consulting Inc.
Toronto

* Denotes NDMA Subcommittee Members

ACES Staff

Eva Kennedy
Scientific and Technical Coordinator

Jan Shwetz
Administrative Assistant

Susan Harder
Technical Assistant